

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1 - 87. Canceled.

88. (New) A coronavirus protein selected from the group consisting of:  
a coronavirus Spike (S) protein, or fragment thereof, having at least 75% amino acid sequence identity with the CRCV S protein whose amino acid sequence is listed in Figure 4, and comprising at least one of the canine respiratory coronavirus (CRCV)- specific amino acids listed in Table 1;

a coronavirus S protein that comprises the amino acid sequence listed in Figure 4, or a variant thereof with at least 97% amino acid sequence identity with the sequence listed in Figure 4;

a coronavirus polymerase (pol) protein, or fragment thereof, having at least 90% amino acid sequence identity with BCV pol protein and comprising the amino acid E at the position corresponding to position 4975 in the BCV genome (Accession No. SWALL:Q91A29);

a coronavirus pol protein that comprises the amino acid sequence listed in Figure 2;

a coronavirus hemagglutinin/esterase (HE) protein, or fragment thereof, having at least 90% amino acid sequence identity with BCV HE protein and comprising one or more of F at position 235, N at position 242 and L at position 253 of the BCV HE protein (Genbank Accession No. AF058942); and

a coronavirus HE protein that comprises the amino acid sequence listed in Figure 14.

89. (New) A polynucleotide that encodes the protein according to Claim 88, or the complement thereof.

90. (New) A polynucleotide according to Claim 89 comprising a nucleotide sequence selected from the group consisting of:
- the nucleotide sequence listed in Figure 3;
  - the nucleotide sequence listed in Figure 1; and
  - the nucleotide sequence listed in Figure 13.
91. (New) A vector comprising the polynucleotide of Claim 89.
92. (New) A host cell comprising the vector of Claim 91.
93. (New) A host cell according to Claim 92 wherein the vector is an expression vector comprising a eukaryotic promoter operatively linked to the polynucleotide, and wherein the host cell is a eukaryotic host cell.
94. (New) A method of obtaining a protein, the method comprising culturing the host cell of Claim 92, expressing the protein in the host cell, and purifying the protein.
95. (New) A method of Claim 94 wherein the protein is selected from the group consisting of
- a coronavirus Spike (S) protein, or fragment thereof, having at least 75% amino acid sequence identity with the CRCV S protein whose amino acid sequence is listed in Figure 4, and comprising at least one of the canine respiratory coronavirus (CRCV)- specific amino acids listed in Table 1; and
  - a coronavirus S protein that comprises the amino acid sequence listed in Figure 4, or a variant thereof with at least 97% amino acid sequence identity with the sequence listed in Figure 4.
96. (New) A protein obtainable by the method of Claim 94.
97. (New) A method of making an anti-CRCV antibody comprising (i) raising an immune response to an S protein or an HE protein according to Claim 88 in an animal and preparing an antibody from the animal or from an immortal cell derived therefrom, or (ii) selecting an antibody from an antibody-display library using an S protein or an HE protein according to Claim 88.

98. (New) A method according to Claim 97 wherein the antibody is to an S protein, further comprising determining whether the antibody has greater affinity for the CRCV S protein than for the BCV S protein.

99. (New) An anti-CRCV antibody obtainable by the method of Claim 98, that has greater affinity for the CRCV S protein than for the BCV S protein.

100. (New) A method according to Claim 97 wherein the antibody is to an HE protein, further comprising determining whether the antibody has greater affinity for the CRCV HE protein than for the BCV HE protein.

101. (New) An anti-CRCV antibody obtainable by the method of Claim 100, that has greater affinity for the CRCV HE protein than for the BCV HE protein.

102. (New) A method of determining whether a dog has been exposed to CRCV, the method comprising:

- (a) obtaining a suitable sample from the dog; and
- (b) identifying CRCV or an anti-CRCV antibody in the sample.

103. (New) A method according to Claim 102 wherein the anti-CRCV antibody is identified using a CRCV, BCV, human coronavirus (HCV) or hemagglutinating encephalomyelitis virus (HEV) antigen.

104. (New) A method according to Claim 102 wherein the suitable sample is an antibody containing sample such as serum, saliva, tracheal wash and bronchiolar lavage.

105. (New) A method according to Claim 102 wherein the suitable sample is a lung wash, tracheal wash, tonsillar swab or a biopsy or post-mortem sample from the respiratory tract of the dog.

106. (New) A method according to Claim 102 wherein the suitable sample is an antibody containing sample, and wherein identifying an anti-CRCV antibody

comprises identifying an antibody that selectively binds to an S protein or to an HE protein.

107. (New) A method according to Claim 106 wherein the S protein is selected from the group consisting of:

- a coronavirus Spike (S) protein, or fragment thereof, having at least 75% amino acid sequence identity with the CRCV S protein whose amino acid sequence is listed in Figure 4, and comprising at least one of the canine respiratory coronavirus (CRCV)- specific amino acids listed in Table 1;

- a coronavirus S protein that comprises the amino acid sequence listed in Figure 4, or a variant thereof with at least 97% amino acid sequence identity with the sequence listed in Figure 4;

- BCV S protein (AF058942);

- HCV S protein (L14643); and

- an S protein with at least 75% amino acid identity with CRCV S protein (Figure 4) or a fragment thereof.

108. (New) A method according to Claim 106 wherein the HE protein is selected from the group consisting of:

- a coronavirus hemagglutinin/esterase (HE) protein, or fragment thereof, having at least 90% amino acid sequence identity with BCV HE protein and comprising one or more of F at position 235, N at position 242 and L at position 253 of the BCV HE protein (Genbank Accession No. AF058942);

- a coronavirus HE protein that comprises the amino acid sequence listed in Figure 14;

- BCV HE protein (AF058942);

- HCV HE protein (M76373); and

- an HE protein with at least 90% amino acid identity with CRCV HE protein (Figure 14) or a fragment thereof.

109. (New) A method according to Claim 102 wherein identifying CRCV comprises identifying a nucleic acid component of CRCV or a protein component of CRCV.

110. (New) A method according to Claim 109 wherein identifying a nucleic acid component of CRCV comprises identifying a polynucleotide that hybridises at high stringency to the BCV genome (AF058942).

111. (New) A method according to Claim 109 wherein the nucleic acid component of CRCV is a polynucleotide that encodes a protein component of CRCV.

112. (New) A method according to Claim 111 wherein the protein component of CRCV is an S protein, a pol protein, or an HE protein.

113. (New) A method according to Claim 112 wherein the S protein is selected from the group consisting of:

a coronavirus Spike (S) protein, or fragment thereof, having at least 75% amino acid sequence identity with the CRCV S protein whose amino acid sequence is listed in Figure 4, and comprising at least one of the canine respiratory coronavirus (CRCV)- specific amino acids listed in Table 1; and

a coronavirus S protein that comprises the amino acid sequence listed in Figure 4, or a variant thereof with at least 97% amino acid sequence identity with the sequence listed in Figure 4.

114. (New) A method according to Claim 112 wherein the pol protein is selected from the group consisting of:

a coronavirus polymerase (pol) protein, or fragment thereof, having at least 90% amino acid sequence identity with BCV pol protein and comprising the amino acid E at the position corresponding to position 4975 in the BCV genome (Accession No. SWALL:Q91A29); and

a coronavirus pol protein that comprises the amino acid sequence listed in Figure 2.

115. (New) A method according to Claim 112 wherein the HE protein is selected from the group consisting of:

a coronavirus hemagglutinin/esterase (HE) protein, or fragment thereof, having at least 90% amino acid sequence identity with BCV HE protein and

comprising one or more of F at position 235, N at position 242 and L at position 253 of the BCV HE protein (Genbank Accession No. AF058942); and  
a coronavirus HE protein that comprises the amino acid sequence listed in Figure 14.

116. (New) A method according to Claim 109 wherein identifying a protein component of CRCV comprises using an antibody reactive with CRCV.

117. (New) A method according to Claim 116 wherein the antibody reactive with CRCV is an anti-BCV antibody, an anti-HCV antibody, or an anti-CRCV antibody.

118. (New) An immunosorbent assay for detecting anti-CRCV antibodies, the assay comprising:

a solid phase coated with a CRCV protein according to Claim 88, or an antigenic fragment thereof, wherein anti-CRCV antibodies in a sample exposed to the solid phase will bind to the protein; and

a detectable label conjugate which will bind to the anti-CRCV antibodies bound to the solid phase.

119. (New) An immunosorbent assay according to Claim 118, wherein the CRCV protein is an S protein or an HE protein.

120. (New) An immunosorbent assay according to Claim 118, wherein the solid phase is a microtitre well.

121. (New) An immunosorbent assay according to Claim 118, wherein the detectable label conjugate comprises anti-dog antibody.

122. (New) An immunosorbent assay according to Claim 118, wherein the detectable label conjugate comprises an enzyme.

123. (New) An immunosorbent assay according to Claim 122, wherein the enzyme is horseradish peroxidase.

124. (New) An immunosorbent assay according to Claim 122, further comprising a substrate for the enzyme.

125. (New) A solid substrate with a CRCV protein according to Claim 88, or an antigenic fragment thereof, attached thereto, for capturing anti-CRCV antibodies from a liquid sample, wherein anti-CRCV antibodies in a sample exposed to the solid substrate will bind to the CRCV protein.

126. (New) A solid substrate according to Claim 125 wherein the CRCV protein is an S protein or an HE protein.

127. (New) A solid substrate according to Claim 125, wherein the solid substrate is a microtitre well.

128. (New) A vaccine composition for vaccinating dogs comprising a coronavirus having an S protein with at least 75% amino acid identity with BCV S protein, or a coronavirus protein having at least 75% amino acid identity with a BCV protein or an immunogenic fragment thereof, or a nucleic acid encoding said coronavirus protein or immunogenic fragment thereof.

129. (New) A vaccine composition according to Claim 128 wherein the coronavirus protein is a BCV, HCV, HEV or CRCV protein, or a modification thereof.

130. (New) A vaccine composition according to Claim 128 wherein the coronavirus protein is an S protein.

131. (New) A vaccine composition according to Claim 130 wherein the S protein is selected from the group consisting of  
a coronavirus Spike (S) protein, or fragment thereof, having at least 75% amino acid sequence identity with the CRCV S protein whose amino acid sequence is listed in Figure 4, and comprising at least one of the canine respiratory coronavirus (CRCV)- specific amino acids listed in Table 1;

a coronavirus S protein that comprises the amino acid sequence listed in Figure 4, or a variant thereof with at least 97% amino acid sequence identity with the sequence listed in Figure 4;

a BCV S protein;

an HCV S protein; and

an HEV S protein,

or an immunogenic fragment thereof.

132. (New) A vaccine composition according to Claim 128 wherein the coronavirus protein is a hemagglutinin-esterase protein (HE) or an integral membrane protein (M).

133. (New) A vaccine composition according to Claim 132 wherein the HE protein is selected from the group consisting of:

a coronavirus hemagglutinin/esterase (HE) protein, or fragment thereof, having at least 90% amino acid sequence identity with BCV HE protein and comprising one or more of F at position 235, N at position 242 and L at position 253 of the BCV HE protein (Genbank Accession No. AF058942);

a coronavirus HE protein that comprises the amino acid sequence listed in Figure 14;

a BCV HE protein;

an HCV HE protein,

or an immunogenic fragment thereof.

134. (New) A vaccine composition according to Claim 128 wherein the coronavirus is selected from BCV, HCV, HEV and CRCV, or a modification thereof.

135. (New) A vaccine composition according to Claim 128 and also comprising a pharmaceutically acceptable adjuvant.

136. (New) A vaccine composition according to Claim 128 further comprising any one or more of:

(a) an agent capable of raising an immune response in a dog against canine parainfluenza virus (CPIV);



(b) an agent capable of raising an immune response in a dog against canine adenovirus type 2 (CAV-2);

(c) an agent capable of raising an immune response in a dog against canine herpesvirus (CHV); and

(d) an agent capable of raising an immune response in a dog against *Bordetella bronchiseptica* (*B. bronchiseptica*).

137. (New) Use of (i) a coronavirus having an S protein with at least 75% amino acid identity with CRCV S protein, or (ii) a coronavirus having an S protein with at least 75% amino acid identity with BCV S protein, or (iii) a coronavirus having an HE protein with at least 90% amino acid identity with CRCV HE protein, or (iv) a coronavirus having an HE protein with at least 90% amino acid identity with BCV HE protein, or (v) a coronavirus protein having at least 75% amino acid identity with a CRCV protein or an immunogenic fragment thereof, or (vi) a coronavirus protein having at least 75% amino acid identity with a BCV protein, or an immunogenic fragment thereof, or (vii) a nucleic acid encoding said coronavirus protein or immunogenic fragment thereof, in the preparation of a medicament for stimulating an immune response against CRCV in a dog or in the preparation of a medicament for prophylaxis of respiratory disease in a dog.

138. (New) Use according to Claim 137 wherein the coronavirus protein is a BCV, HCV, HEV or CRCV protein, or a modification thereof.

139. (New) Use according to Claim 137 wherein the coronavirus protein is an S protein.

140. (New) Use according to Claim 139 wherein the S protein is selected from the group consisting of

a coronavirus Spike (S) protein, or fragment thereof, having at least 75% amino acid sequence identity with the CRCV S protein whose amino acid sequence is listed in Figure 4, and comprising at least one of the canine respiratory coronavirus (CRCV)- specific amino acids listed in Table 1;

a coronavirus S protein that comprises the amino acid sequence listed in Figure 4, or a variant thereof with at least 97% amino acid sequence identity with the sequence listed in Figure 4;

a BCV S protein; and

an HCV S protein,

or an immunogenic fragment thereof.

141. (New) Use according to Claim 137 wherein the coronavirus protein is HE or M.

142. (New) Use according to Claim 141 wherein the HE protein is selected from the group consisting of:

a coronavirus hemagglutinin/esterase (HE) protein, or fragment thereof, having at least 90% amino acid sequence identity with BCV HE protein and comprising one or more of F at position 235, N at position 242 and L at position 253 of the BCV HE protein (Genbank Accession No. AF058942);

a coronavirus HE protein that comprises the amino acid sequence listed in Figure 14;

a BCV HE protein;

an HCV HE protein,

or an immunogenic fragment thereof.

143. (New) Use according to Claim 137 wherein the coronavirus is selected from BCV, HCV, HEV and CRCV, or a modification thereof.

144. (New) A method of vaccinating a dog against CRCV, the method comprising administering to the dog a vaccine composition according to Claim 128.

145. (New) A method for combating the spread of CRCV between dogs comprising determining whether a dog is infected with CRCV according to the method of Claim 102 and, if the dog is infected with CRCV, quarantining the dog.

146. (New) A method for combating the spread of CRCV between dogs comprising determining whether a dog is infected with CRCV according to the

method of Claim 102 and, if the dog is infected with CRCV, vaccinating other dogs that have been, are, or are likely to be in contact with the dog.

147. (New) A method for identifying a test vaccine capable of preventing canine infectious respiratory disease (CIRD) in dogs, comprising

- (a) determining whether a dog has been exposed to CRCV according to the method of Claim 102,
  - (b) if the dog has not been exposed to CRCV, administering a test vaccine to the dog,
  - (c) inoculating the dog with CRCV, and
  - (d) determining whether the dog develops CIRD,
- wherein the absence of CIRD in step (d) indicates that the test vaccine is capable of preventing CIRD.

148. (New) A vaccine identified by the method of Claim 147.

149. (New) An *E. coli* strain Spike D-1 CRCV, containing a plasmid whose insert contains a portion of the CRCV S cDNA, as deposited by the Royal Veterinary College at the NCIMB under Accession number NC1MB 41146 on 25 July 2002.

150. (New) A plasmid contained in *E. coli* strain Spike D-1 CRCV, deposited by the Royal Veterinary College at the NCIMB under Accession number NCIMB 41146 on 25 July 2002.

151. (New) A kit of parts for the immunosorbent assay according to Claim 118, comprising a solid phase, a CRCV or CRCV-like S protein and/or a CRCV or CRCV-like HE protein for coating the solid phase, and a detectable label conjugate.

152. (New) A kit of parts according to Claim 151 wherein the solid phase comprises a microtitre plate.

153. (New) A kit of parts according to Claim 151 wherein the detectable label conjugate comprises an anti-dog antibody.

154. (New) A kit of parts according to Claim 151 wherein the detectable label conjugate comprises an enzyme.
155. (New) A kit of parts according to Claim 154 further comprising a substrate for the enzyme.
156. (New) A kit of parts according to Claim 151 further comprising a positive control sample that contains an anti-CRCV S protein antibody and/or an anti-CRCV HE protein antibody.
157. (New) A method of passively immunising a dog against CRCV, comprising administering an antibody that reacts with CRCV to the dog.
158. (New) A method according to Claim 157 wherein the antibody that reacts with CRCV comprises an anti-BCV antibody, an anti-HCV antibody, or an anti-CRCV antibody.
159. (New) A method according to Claim 157 wherein the antibody that reacts with CRCV comprises an anti-S protein antibody or an anti-HE protein antibody.
160. (New) Use of an antibody that reacts with CRCV in the preparation of a medicament for passively immunising a dog against CRCV.
161. (New) Use according to Claim 160 wherein the antibody that reacts with CRCV is an anti-BCV antibody, an anti-HCV antibody, or an anti-CRCV antibody.
162. (New) Use according to Claim 160 wherein the antibody that reacts with CRCV is an anti-S protein antibody or an anti-HE protein antibody.
163. (New) A method of diagnosing CIRD, the method comprising determining whether a dog has been exposed to CRCV according to the method of Claim 102.